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No. 17-290

IN THE

Supreme Court of the United States

MERCK SHARP & DOHME CORP.,

Petitioner,

v.

DORIS ALBRECHT, ET AL.,

Respondents.

On Petition For A Writ Of Certiorari To The United States Court Of Appeals For The Third Circuit

REPLY IN SUPPORT OF PETITION FOR A WRIT OF CERTIORARI

SHAY DVORETZKY
Counsel of Record
YAAKOV M. ROTH
JEFFREY R. JOHNSON
JONES DAY
51 Louisiana Ave., NW
Washington, DC 20001
(202) 879-3939
sdvoretzky@jonesday.com

Counsel for Petitioner

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TABLE OF CONTENTS

Page

I. RESPONDENTS DEFEND THE THIRD CIRCUIT'S RULING ONLY BY MISCHARACTERIZING IT 2

II. THIS CASE REMAINS AN IDEAL VEHICLE FOR CLARIFYING THE SCOPE OF A CRITICAL DEFENSE 9

CONCLUSION 12

TABLE OF AUTHORITIES

Page(s)

CASES

Boyle v. United Techs. Corp.,
487 U.S. 500 (1988) 8

In re Celexa & Lexapro Mktg. & Sales Practices Litig.,
779 F.3d 34 (1st Cir. 2015) 9

Markman v. Westview Instruments, Inc.,
517 U.S. 370 (1996) 8

Miller v. Fenton,
474 U.S. 104 (1985) 8

PLIVA, Inc. v. Mensing,
564 U.S. 604 (2011) 1, 10

Ramsey v. United Mine Workers of Am.,
401 U.S. 302 (1971) 7

Reckis v. Johnson & Johnson,
28 N.E.3d 445 (Mass. 2015) 9

Santosky v. Kramer,
455 U.S. 745 (1982) 7

Wyeth v. Levine,
555 U.S. 555 (2009) 1, 2, 9, 10

STATUTES

21 U.S.C. § 355 6

OTHER AUTHORITIES

21 C.F.R. § 314.100 4

The decision below guts the preemption defense recognized in *Wyeth v. Levine*, 555 U.S. 555 (2009). Merck told the FDA everything it knew about the possible link between Fosamax and atypical femur fractures. It proposed to change the label to warn of that risk. But the FDA rejected that proposal and cast doubt on the underlying science. The Third Circuit *accepted all of this*, yet still let Respondents' failure-to-warn claims proceed. Absent a "smoking gun," the court reasoned, a lay jury must muse about whether the FDA—neglecting its *own* legal duties—rejected Merck's proposal exclusively for semantic reasons and thus might conceivably have approved an alternative warning satisfying state law.

Under *Levine*, the FDA's rejection of a proposed warning is preemptive. *Id.* at 571-72. And, under *PLIVA, Inc. v. Mensing*, "conjecture[]" does not "suffice" to defeat the defense. 564 U.S. 604, 621 (2011). Accordingly, if a manufacturer shares its data on a risk, proposes to warn of it, and is rebuffed, the case is over. There is no room for a jury to deconstruct the FDA's decision or speculate about an infinite array of counterfactuals. Nonetheless, courts have—through a line of decisions culminating in the one below—made it all but impossible for drug manufacturers to navigate FDA oversight while still protecting themselves against massive tort liability.

Respondents barely dispute Merck's view of the law. Instead, they purport to reconcile it with the decision below, by mischaracterizing the record and misrepresenting the court's rationale. But the Third Circuit understood the relevant facts—that Merck proposed a warning about the risk at issue; that the FDA said no, with no wriggle room; and that the

FDA expressed skepticism on the science both before and for 18 months after the rejection. Its legal holding—based on an artificially heightened burden of proof, deference to juries on matters of regulatory process, and a skewed understanding of *Levine*—was that *not even this* suffices to trigger preemption. Respondents cannot hide from those legal errors.

Respondents' other ground for denying review is their assertion that this case is a poor vehicle. Quite the opposite. The Third Circuit's aggressive holding turns the FDA's authority over to 500-plus juries in the underlying MDL alone, not to mention its systemic effect on this important area of law. As for Respondents' half-hearted "alternative ground" to affirm, the court below did not pass upon it, so it is no excuse to shield from review what the court *did* decide. And Merck's agreement on the need for a warning simply highlights the inequity of the Third Circuit's rule: Even a manufacturer doing its best to warn the public can be stymied by federal regulation and then hit with enormous state-law liability.

I. RESPONDENTS DEFEND THE THIRD CIRCUIT'S RULING ONLY BY MISCHARACTERIZING IT

A. It is untenable to hold manufacturers liable for failure-to-warn under state law even when they (i) sought approval to issue a warning and (ii) were told "no" by a federal regulator that (iii) viewed the science differently. Pet.28-30. Respondents do not appear to disagree with that legal rule. They instead suggest, through selective and misleading accounts of the record, that the Third Circuit did not hold otherwise. But the court below was very clear: It denied summary judgment to Merck *despite* these facts, not by *disputing* them.

First, Respondents insist that Merck "never proposed" warning about the relevant risk ("atypical femoral fractures"), but "only about a different risk—minor stress fractures." Opp.1-2; *see also* Opp.i, 18.

That incredible revisionism was *not* a basis of the decision below. Rather, the Third Circuit recognized that Merck had informed the FDA about "possible connections between long-term bisphosphonate use and *atypical femoral fractures*," and had proposed a warning about "[l]ow-energy *fractures* of the subtrochanteric and proximal *femoral shaft*." Pet.App.13a, 15a (emphases added). The FDA's response letter, likewise, described Merck's proposed warning as concerning "low-energy fractures at the subtrochanteric region of the femoral shaft." C.A.App.1500. Given all this, it is no wonder that the court below readily acknowledged that Merck's proposal "address[ed] atypical femoral fractures," Pet.App.15a, not "minor stress fractures."

Ignoring these facts, Respondents note that Merck's proposal alternatively described the fractures in question as "stress fractures." Opp.7. So what? Merck's proposal was *titled* "**Low-Energy Femoral Shaft Fracture**," and it grew out of a back-and-forth with the agency that centered on such fractures. Pet.App.13a-15a. Moreover, these femoral fractures *are* a particular example of stress fracture, C.A.App.A2013, and even if the FDA found that language confusing, there was no doubt that Merck's warning related to the very risk at issue in these cases, as the court below acknowledged.

Second, Respondents claim that the FDA merely asked Merck to *revise* its proposed warning, and that Merck "rebuffed" its "repeated entreaties." Opp.8.

This rewriting of history is worse than the last. Respondents selectively quote an FDA letter that offered to "work with" Merck on "atypical fracture language, if it is warranted," Pet.App.17a-18a—but they ignore the part of the letter that asked Merck to "*hold off*" on adding any fracture-related language so that the agency could "close out" Merck's PAS and *then* investigate—with Merck and the FDA's Office of Surveillance and Epidemiology—whether a warning was "warranted," C.A.App.A1498 (emphasis added). Far from inviting Merck to *revise* its proposal, the FDA asked Merck to *drop* it. And, again, the court below so recognized, recounting how the FDA firmly stated that it was "not prepared to include language about low-energy femoral fractures in the Warnings and Precautions section of the label." Pet.App.17a.

Respondents retort that the complete response letter "invited [Merck] to 'resubmit' its application." Opp.8. But the word "resubmit" appears only in a boilerplate recitation of regulatory options: "Within one year after the date of this letter, you are required to resubmit or take one of the other actions available under 21 CFR 314.110." C.A.App.A1501. This did not "entreat" Merck to do anything, Opp.8, and the Third Circuit never mentioned it, much less relied on it. Had the FDA wanted Merck to rephrase, it was obligated to say so: "When possible, a complete response letter will recommend actions that the applicant might take to place the application ... in condition for approval." 21 C.F.R. § 314.100(a)(4).

Finally, Respondents insist that the FDA never articulated any doubts about the science, and instead expressly rejected Merck's proposal merely based on minor wording quibbles. Opp.18-20.

Once again, however, the Third Circuit acknowledged the "force" of the undisputed facts. Pet.App.62a. Among other things:

- Before denying Merck's request, the FDA asked Merck to "hold off" pending further research by agency scientists into whether a warning was "warranted," Pet.App.17a-18a;
- After denying Merck's request, the FDA announced that, as the data had "not shown a clear connection between bisphosphonate use and ... femur fractures," it would "gather additional information" through an "outside expert task force," Pet.App.19a; and
- After that task report issued a report, the FDA declared it was "confident that atypical femur fractures are potentially more closely related" to bisphosphonate use than it "previously had evidence for," and required manufacturers to add warnings, Pet.App.21a.

Respondents largely ignore this evidence, instead declaring (*e.g.*, Opp.2, 16-17, 20-21, 32) that Merck's case "hinged" on hearsay notes of a call on which the FDA said the "conflicting nature of the literature d[id] not provide a clear path forward," Pet.App.17a. Merck's counsel's identification of those notes at oral argument hardly makes them Merck's *only* evidence. In fact, the entire above timeline—with which those notes are consistent—proves the point.

Respondents further assert that the FDA *must* have rejected the proposal solely based on language quibbles, as its complete response letter mentioned stress-fracture language yet allegedly did not quarrel with the underlying science. Opp.16, 18-19. Again,

however, Respondents just ignore the evidence they dislike. The response letter provided "*reasons*" for the rejection—plural—and its *very first* was that Merck's proffered "*justification* for the proposed **PRECAUTIONS** section language is inadequate." Pet.App.18a (emphases added). That is, the agency was not persuaded by the scientific case that must justify any label change. Whatever issues it had with the term "stress fracture"—identified *separately* in the letter's *next* sentence—scientific doubt was an independent ground for rejection.

This understanding of the response letter is the only one that comports with the FDA's other actions (such as asking Merck to "hold off," and working with the task force) and the only one reconcilable with the FDA's own legal duties. The FDA *must* "initiate discussions to reach agreement on ... the content[]" of "label changes" if it "becomes aware of new safety information" justifying such a change, 21 U.S.C. § 355(o)(4)(A), (C)—a duty that Respondents neither dispute nor address. The FDA indisputably was aware of all of the safety information related to this issue. Thus, if the FDA believed that a warning was scientifically justified, it was obligated to work with Merck to craft one. That is precisely what the FDA did 18 months later, when it deleted "every instance" of use of the term "stress fractures" from Merck's post-task force proposal. Pet.App.22a. Its failure to do the same in 2009 belies Respondents' narrative.

B. Respondents try to downplay the reach of the decision below not only by muddying the facts on the substantive preemption issue, but also by misstating the court's legal holdings on two related points.

First, while Respondents admit that the Third Circuit decision requires manufacturers to prove preemption by clear and convincing evidence, Opp.24, they maintain that the "application of a preponderance standard would have made no difference" here, because of the supposed "weakness of [Merck's] evidence," Opp.25. Even setting aside their grossly misleading description of that evidence, *see supra* pp. 3-6, that is wrong. The Third Circuit *itself* tied its conclusion to its clear-and-convincing-evidence standard. It acknowledged Merck's strong case, *e.g.*, Pet.App.62a, but held that, because the standard of proof is "[c]rucial[]," Merck had to prove that no rational juror could find the odds of rejection "something less than highly probable," Pet.App.58a; *see also* Pet.App.55a (demanding a "smoking gun"). Merck fell short solely because it could not meet that "heightened standard." Pet.App.68a.[1]

Second, Respondents suggest that the Third Circuit's other crucial legal conclusion—that a *jury* must determine whether the FDA would have approved the requested warning—was limited to the "circumstances of this case" because Merck sought to

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[1] Respondents only halfheartedly defend the circuit court's standard of proof, Opp.24-25, and Merck already distinguished the authority on which they rely, Pet.25-28. Respondents' only new case applied a *statute* dictating a "clear proof" test, *Ramsey v. United Mine Workers of Am.*, 401 U.S. 302, 309 (1971), in no way supporting a judge-made heightened-proof rule here. As for the notion that such a standard is appropriate because the preemption defense rests on "speculation," that misses the point. Absent a congressional directive, cases seeking money damages simply are not important enough to justify burdening one side with more of the risk of error, regardless of the *source* of that risk. *See Santosky v. Kramer*, 455 U.S. 745, 755 (1982).

rely on evidence outside the "official regulatory record." Opp.26. Not so. The Third Circuit held, as a *categorical* matter, that "whether the FDA would have rejected a proposed label change is a question of fact that must be answered by a jury." Pet.App.38a; *see id.* at 39a-54a. In doing so, the court rejected not only Merck's view on that issue, but *Respondents'* view that "judicial decisionmaking is required when a preemption determination" includes evaluation of a complete response letter. Pet.App.52a. Under the Third Circuit's remarkable holding, the jury in *all* circumstances presumptively determines the applicability of the legal preemption defense through an "evaluative inference about human behavior," which it should base on "correspondence, agency statements, contemporaneous medical literature, the requirements of the CBE regulation, and whatever intuitions [it] may have about administrative inertia and agency decision-making." Pet.App.54a.[2]

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[2] Again, Respondents' defense of the Third Circuit's rule on the merits is muted at best. The law-soaked question whether the FDA would have approved a particular warning differs significantly from the question whether equipment conformed to government specifications, *see Boyle v. United Techs. Corp.*, 487 U.S. 500, 512-14 (1988). This Court has regularly left such questions for judges, not juries. *See, e.g.*, *Markman v. Westview Instruments, Inc.*, 517 U.S. 370 (1996) (construing disputed terms of art in a patent); *Miller v. Fenton*, 474 U.S. 104 (1985) (whether confession was "voluntary").

II. This Case Remains an Ideal Vehicle for Clarifying the Scope of a Critical Defense

A. This Court's guidance is needed on how to apply what the Third Circuit called *Levine*'s "cryptic," "open-ended" statement about "clear evidence." Pet.App.28a. Respondents insist that this Court should deny review because no square circuit split exists. Opp.13. But this Court has reviewed even one-off erroneous preemption decisions because of the "importance of the ... issue," *Levine*, 555 U.S. at 563. Where, as here, lower courts have gone off-course *en masse*, Pet.18-25, review is even more obviously warranted.

Respondents respond that, in fact, courts uphold preemption defenses on occasion. Opp.15. The cases they cite, however, only highlight the lower courts' stingy application of *Levine*: limiting the defense to scenarios where the FDA rejected a *nearly identical* warning, *expressly* for policy reasons. Pet.20-22; *e.g.*, *Reckis v. Johnson & Johnson*, 28 N.E.3d 445, 458-59 (Mass. 2015) (no preemption for failure to warn of "life-threatening disease," even though FDA rejected warning for "life-threatening diseases, including [three named ones]," because the rejection "could well have" stemmed from the naming of specific diseases).[3] That is obviously not the only situation

[3] Ironically, Respondents also cite a decision, pending on appeal in the Ninth Circuit, where *Respondents' counsel* is seeking reversal *based on the decision below*. Opp.15. They also cite *In re Celexa & Lexapro Marketing & Sales Practices Litigation*, 779 F.3d 34 (1st Cir. 2015), but that decision found preemption because the absence of "newly acquired information" precluded the manufacturer from changing its label unilaterally, not because the FDA would have rejected a change. *Id.* at 41-43.

in which the FDA "would have prevented" the manufacturer from adding a warning, *Levine*, 555 U.S. at 573, and yet lower courts have wrongly made that the bar.

B. Respondents next object that this case would not be a good vehicle to clarify preemption law. But, if anything, their arguments only highlight the need for guidance in this field.

First, Respondents claim that they have *other* claims against Merck that may not be affected by the resolution of this case. Opp.30-32. Actually, most of those are failure-to-warn claims by another name; the district court dismissed them as just derivative (Pet.App.139a-46a); the Third Circuit revived them only because it revived the central failure-to-warn claims (Pet.App.74a). Meanwhile, by virtue of the Third Circuit decision, Merck faces the prospect of more than 500 individual trials at which *different* juries must speculate about whether the FDA would have approved a marginally rephrased warning.

Moreover, this particular MDL aside, Merck and every other pharmaceutical manufacturer must now innovate in the shadow of the Third Circuit's indefensible legal rules. This Court has not hesitated before to grant interlocutory review in such circumstances. *See Mensing*, 564 U.S.at 610-11.

Second, Respondents threaten that they "may"—"may"—"raise the district court's [alleged] violations of their procedural rights" as an alternative ground for affirmance. Opp.29. They admit, however, that the Third Circuit "did not ... reach [their] procedural objections." *Id.* At most, their (non-jurisdictional) complaints are thus a matter for eventual remand.

In any event, the district court's show-cause procedure was perfectly proper. Many courts have followed similar procedures when addressing cross-cutting issues in the MDL context, and the district court gave Respondents chance after chance to develop their arguments. Pet.App.135a-36a.

There is no genuine risk that the record relevant to the preemption issue is "underdeveloped." Opp.30. Respondents cite just one example of an allegedly "missing" fact—deposition testimony from Ms. Merritt, the Merck employee who took the notes of the FDA phone call that Respondents claim are the linchpin of Merck's case. That is specious, both because the notes are hardly central to the outcome, *supra* p. 5, and because Respondents offer no basis to doubt that they accurately recount the call. Plus, given the many opportunities they had to seek this evidence, Respondents' "failure" to do so "is no [one's] fault other than" their own. Pet.App.136a.

Third, Respondents press the strange argument that, because all *now* agree that bisphosphonate labels should warn about atypical femoral fractures, the dangerous policy implications of unrestrained failure-to-warn claims are somehow absent here. Opp.27-28. That simply does not follow. Before the task force report, the FDA did not believe there was enough evidence to warn about atypical femoral fractures. *Supra* pp. 5-6. Respondents seek to upset that expert decision by asking juries to penalize Merck for having failed to warn *during that period*. Indeed, this case highlights the no-good-deed-goes-unpunished nature of the decision below: Merck faces liability even though it *tried* to warn of a developing risk and was rebuffed.

Furthermore, the Third Circuit's decision will create havoc in *other* cases. Its clear-and-convincing-evidence standard will by definition supplant the FDA's judgment with a jury's, defeating preemption even where it is shown (by a preponderance) that the FDA would have rejected a warning. Similarly, the Third Circuit's demand for a "'smoking gun' rejection letter," Pet.App.55a, will produce a wasteful flurry of requests to add alternatively phrased warnings. These are compelling reasons for review that have nothing to do with Fosamax. Of course, if the Court has any doubt about these policy implications, it could solicit the FDA's views.

Finally, Respondents do not dispute the need for another "stake in the ground" to help lower courts, but argue that Merck's "evidence is weak." Opp.32. Repeating this bogus claim does not make it true. If a manufacturer can be liable even after telling the FDA about the risk, proposing an on-point label, and being turned down while the FDA expressed concerns about the science, *Levine*'s preemption defense might as well not exist at all.

CONCLUSION

The petition should be granted.

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SHAY DVORETZKY
Counsel of Record
YAAKOV M. ROTH
JEFFREY R. JOHNSON
JONES DAY
51 Louisiana Ave., NW
Washington, DC 20001
(202) 879-3939
sdvoretzky@jonesday.com

Counsel for Petitioner